

AMENDMENTS TO THE CLAIMS

Claims 1-4 (**cancelled**)

5. (**currently amended**) A method of determining the identification of a nucleotide at a detection position in a target sequence comprising a first target domain adjacent to said detection position and a second target domain comprising said detection position, wherein said method comprises:

a) hybridizing a first ligation probe to said first target domain, said first ligation probe comprising:

- i) a first portion comprising an upstream universal priming site (UUP); and
- ii) a second portion comprising a first target-specific sequence comprising a first base at an interrogation position; and

b) hybridizing a second ligation probe to said second target domain, said second ligation probe comprising:

- i) a third portion comprising a downstream universal priming site (DUP); and
- ii) a fourth portion comprising a second target-specific sequence;

wherein if said first base is perfectly complementary to said nucleotide at said detection position, a ligation complex is formed, and

wherein at least one of said first and second ligation probes comprises a fifth portion comprising an adapter sequence;

- c) removing non-hybridized probes;
- d) providing a ligase that ligates said first and second ligation probes to form a ligated probe;
- e) amplifying said ligated probe using said UUP and said DUP to generate a plurality of amplicons;
- f) contacting said amplicons with an array of capture probes; and
- g) determining the nucleotide at said detection position.

Claims 6-8 (**cancelled**)

9. (**previously amended**) A method according to claim 5 , 26, 32 and 33 wherein said removing comprises:

- a) enzymatically adding a binding ligand to said target sequence to form a target sequence comprising said binding ligand;

b) binding a hybridization complex comprising said target sequence comprising said binding ligand to a binding partner immobilized on a solid support;

c) washing away unhybridized probes; and

d) eluting said probes off said solid support.

10. **(previously amended)** A method according to claim 5, 26, 32, or 33 wherein said removing is done using a double-stranded specific moiety.

11. **(original)** A method according to claim 10 wherein said double-stranded specific moiety is an intercalator attached to a support.

12. **(previously amended)** A method according to claim 11 wherein said support is a bead.

13. **(previously amended)** A method according to claim 5, 26, 32, or 33 wherein said amplifying is done by:

a) hybridizing a first universal primer to said UUP;

b) providing a polymerase and dNTPs such that said first universal primer is extended;

c) hybridizing a second universal primer to said DUP;

d) providing a polymerase and dNTPs such that said second universal primer is extended;

and

e) repeating steps a) through d).

14. **(previously amended)** A method according to claim 5, 26, 32, or 33 wherein said array comprises:

a) a substrate with a patterned surface comprising discrete sites; and

b) a population of microspheres comprising at least a first subpopulation comprising a first capture probe and a second subpopulation comprising a second capture probe.

15. **(original)** A method according to claim 14 wherein said discrete sites comprise wells.

16. **(previously amended)** A method according to claim 14 wherein said substrate comprises a fiber optic bundle.

Claims 17-18 **(canceled)**

19. **(previously amended)** A method according to claim 5 or 32, further comprising providing a support on which the target sequence is immobilized.

20. **(original)** A method according to claim 19, wherein said non-hybridized probes are removed without removing said target sequence from said support.

21. **(previously amended)** A method according to claim 5 or 32, further comprising attaching said target sequence to a support.

22. **(currently amended)** A method according to claim 21, wherein said target sequence is attached to said support by a method selected from the group consisting of labeling said target sequence with a functional attachment moiety capable of binding to that binds said support and interacting said functional attachment moiety with said support, absorption of said target sequence on ~~a charged support~~ said support wherein said support comprises charged groups, direct chemical attachment of said target sequence to said support and photocrosslinking said target sequence to said support.

23. **(previously amended)** A method according to claim 9, wherein said support is selected from the group consisting of paper, plastic and tubes.

Claims 24-25 **(cancelled)**

26. **(currently amended)** A method of determining the identification of a nucleotide at a detection position in a target sequence comprising a first target domain adjacent to said detection position and a second target domain comprising said detection position, wherein said method comprises:

a) providing a support on which the target sequence is immobilized;

b) hybridizing a first ligation probe to said first target domain, said first ligation probe comprising:

i) a first portion comprising an upstream universal priming site (UUP); and

ii) a second portion comprising a first target-specific sequence comprising a first base at an interrogation position; and

c) hybridizing a second ligation probe to said second target domain, said second ligation probe comprising:

i) a third portion comprising a downstream universal priming site (DUP); and

ii) a fourth portion comprising a second target-specific sequence;

wherein if said first base is perfectly complementary to said nucleotide at said detection position, a ligation complex is formed, and wherein at least one of said first and second ligation probes comprises a fifth portion comprising an adapter sequence;

d) removing non-hybridized probes;

- e) providing a ligase that ligates said first and second ligation probes to form a ligated probe;
- f) amplifying said ligated probe using said UUP and said DUP to generate a plurality of amplicons;
- g) contacting said amplicons with an array of capture probes; and
- h) determining the nucleotide at said detection position.

Claims 27-29 (**cancelled**)

30. (**previously added**) A method according to claim 9 wherein said solid support is a bead.

31. (**previously added**) A method according to claim 26 wherein said non-hybridized probes are removed without removing said target sequence from said support.

32. (**currently amended**) A method of determining the identification of a nucleotide at a detection position in a target sequence comprising a first target domain comprising said detection position and a second target domain adjacent to said detection position, wherein said method comprises:

a) hybridizing a first ligation probe to said first target domain, said first ligation probe comprising:

- i) a first portion comprising an upstream universal priming site (UUP);
- ii) a second portion comprising a first target-specific sequence; and
- iii) an interrogation position that is complementary to said detection position; and

b) hybridizing a second ligation probe to said second target domain, said second ligation probe comprising:

- i) a third portion comprising a downstream universal priming site (DUP); and
- ii) a fourth portion comprising a second target-specific sequence;

whereby if said interrogation position of said first probe is perfectly complementary to said nucleotide at said detection position, a ligation complex is formed, and wherein at least one of said first and second ligation probes comprises a fifth portion comprising an adapter sequence;

- c) removing non-hybridized probes;
- d) providing a ligase that ligates said first and second ligation probes to form a ligated probe;
- e) amplifying said ligated probe using said UUP and said DUP to generate a plurality of amplicons;

- f) contacting said amplicons with an array of capture probes; and
- g) determining the nucleotide at said detection position.

33. **(currently amended)** A method of determining the identification of a nucleotide at a detection position in a target sequence comprising a first target domain comprising said detection position and a second target domain adjacent to said detection position, wherein said method comprises:

- a) providing a support on which the target sequence is immobilized;
- b) hybridizing a first ligation probe to said first target domain, said first ligation probe comprising:

- i) a first portion comprising an upstream universal priming site (UUP);
- ii) a second portion comprising a first target-specific sequence; and
- iii) an interrogation position; and

- c) hybridizing a second ligation probe to said second target domain, said second ligation probe comprising:

- i) a third portion comprising a downstream universal priming site (DUP); and
- ii) a fourth portion comprising a second target-specific sequence;

whereby if said interrogation position of said first probe is perfectly complementary to said nucleotide at said detection position, a ligation complex is formed, and wherein at least one of said first and second ligation probes comprises a fifth portion comprising an adapter sequence;

- d) removing non-hybridized probes;
- e) providing a ligase that ligates said first and second ligation probes to form a ligated probe;
- f) amplifying said ligated probe using said UUP and said DUP to generate a plurality of amplicons;
- g) contacting said amplicons with an array of capture probes; and
- h) determining the nucleotide at said detection position.

34. **(previously added)** A method according to claim 15, wherein said substrate comprises a fiber optic bundle.

35. (New) The method according to claim 22, wherein said target sequence is attached to said support by labeling said target sequence with a functional attachment moiety capable of binding to said support and interacting said functional attachment moiety with said support.
36. (New) The method according to claim 22, wherein said target sequence is attached to said support by absorption of said target sequence on said support wherein said support comprises charged groups.
37. (New) The method according to claim 22, wherein said target sequence is attached to said support by direct chemical attachment of said target sequence to said support.
38. (New) The method according to claim 22, wherein said target sequence is attached to said support by photocrosslinking said target sequence to said support.